This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A method of determining the specific residues binding to a target of interest, such residues being within a known parent polypeptide that binds to the target of interest, comprising the steps of:

(a) providing a known parent polypeptide with a known primary structure, such primary structure consisting of n residues, which parent polypeptide ~~that~~ binds to a target of interest ~~with a known primary structure, such primary structure consisting of n residues~~;

(b) constructing a first peptide of the formula R_1-Z-R_2,

wherein

R_1 comprises from 2 to n residues, such residues the same as or homologs of residues in the parent polypeptide and in the same order as residues in the parent polypeptide primary structure;

Z is a residue or mimetic thereof providing both a nitrogen atom (N) and a sulfur atom (S) for metal ion complexation;

R_2 comprises from 0 to n - 2 residues, such residues the same as or homologs of residues in the parent polypeptide and in the same order as residues in the parent polypeptide primary structure, and forming with R_1 a sequence in the same order as in the parent polypeptide primary structure with Z either inserted between two adjacent residues corresponding to two adjacent residues in such primary structure or substituting for a single residue corresponding to a single residue in such primary structure, and wherein the residues comprising R_1-Z-R_2 are equal to either n or n +1;

(c) complexing the first peptide of the formula R_1-Z-R_2 to a metal ion, thereby forming a first R_1-Z-R_2 metallopeptide;

(d) screening the first R_1-Z-R_2 metallopeptide for binding to the target of interest;

(e) repeating steps (b) through (d), wherein the resulting R_1-Z-R_2 metallopeptide differs in at least either R_1 or R_2; and

(f) selecting the R_1-Z-R_2 metallopeptide exhibiting substantially decreased binding to the target of interest, whereby at least one residue of the sequence binding to the metal ion of such R_1-Z-R_2 metallopeptide comprises the identification of the specific residues of the parent polypeptide binding to the target of interest.

2. (Original) The method of claim 1 wherein Z is an L- or D-3-mercapto amino acid.

3. (Original) The method of claim 2 wherein the L- or D-3-mercapto amino acid is L- or D-cysteine, L- or D-penicillamine, 3-mercapto phenylalanine, or a homolog of any of the foregoing.

4. (Original) The method of claim 1 wherein the metal ion is an ion of V, Mn, Fe, Co, Ni, Cu, Zn, Ga, As, Se, Y, Mo, Tc, Ru, Rh, Re, Pd, Ag, Cd, In, Sn, W, Re, Os, Ir, Pt, Au, Hg, Tl, Pb, Bi, Po, At, Sm, Eu or Gd.

5. (Original) The method of claim 1 wherein the target of interest is a receptor, antibody, toxin, enzyme, hormone, nucleic acid, intracellular protein domain of biological relevance or extracellular protein domain of biological relevance.

6. (Original) The method of claim 1 wherein screening for binding to the target of interest comprises competing a known binding partner for binding to the target of interest with the R_1-Z-R_2 metallopeptide.

7. (Original) The method of claim 6 wherein the known binding partner is the parent polypeptide.

8. (Original) The method of claim 1 wherein screening for binding to the target of interest comprises a functional assay.

9. (Original) The method of claim 1 wherein the target of interest is a biological

receptor capable of transmitting a signal, and screening further comprises determining whether the R_1-Z-R_2 metallopeptide induces decreased transmission of the signal.

10. (Original) A method of determining the specific residues binding to a target of interest within a known primary sequence parent polypeptide that binds to the target of interest, comprising the steps of:

(a) making a series of peptides, wherein each peptide in the series includes the known primary sequence of the parent polypeptide and a single inserted L- or D-3-mercapto amino acid residue, with the single L- or D-3-mercapto amino acid inserted for each peptide at each position along the primary sequence from the position between the second and third residues from the N-terminus through the C-terminus position;

(b) complexing each peptide in the series with a metal ion to form a series of metallopeptides; and,

(c) determining the binding of each metallopeptide of the series of metallopeptides to the target of interest.

11. (Original) The method of claim 10, further comprising the step of selecting the metallopeptide or metallopeptides of the series exhibiting substantially decreased binding to the target of interest.

12. (Original) The method of claim 10, wherein any L- or D-3-mercapto amino acid residue in the series of peptides other than the single inserted L- or D-3-mercapto amino acid residue further comprises a sulfur protecting group, whereby the sulfur therein cannot complex a metal ion.

13. (Original) The method of claim 10, wherein any L- or D-3-mercapto amino acid residue in the series of peptides other than the single inserted L- or D-3-mercapto amino acid residue is substituted with a homolog.

14. (Original) The method of claim 10, wherein for any peptide in the series containing

a proline residue as either of the two residues on the immediately adjacent N-terminus side of the single inserted L- or D-3-mercapto amino acid residue, the proline residue is substituted with a homolog.

15. (Original) The method of claim 10, wherein the L- or D-3-mercapto amino acid is L- or D-cysteine, L- or D-penicillamine, 3-mercapto phenylalanine, or a homolog of any of the foregoing.

16. (Original) The method of claim 10, wherein the metal ion is an ion of V, Mn, Fe, Co, Ni, Cu, Zn, Ga, As, Se, Y, Mo, Tc, Ru, Rh, Re, Pd, Ag, Cd, In, Sn, W, Re, Os, Ir, Pt, Au, Hg, Tl, Pb, Bi, Po, At, Sm, Eu or Gd.

17. (Original) The method of claim 16, wherein the metal ion is an ion of technetium or rhenium.

18. (Original) The method of claim 10 wherein the target of interest is a receptor, antibody, toxin, enzyme, hormone, nucleic acid, intracellular protein domain of biological relevance or extracellular protein domain of biological relevance.

19. (Original) The method of claim 10, wherein determining the binding of each metallopeptide of the series of metallopeptides to the target of interest comprises competing a known binding partner for binding to the target of interest with each metallopeptide.

20. (Original) The method of claim 10, wherein determining the binding of each metallopeptide of the series of metallopeptides to the target of interest comprises a functional assay.

21. (Original) The method of claim 10, wherein the target of interest is a biological receptor capable of transmitting a signal, and wherein determining the binding of each metallopeptide of the series of metallopeptides to the target of interest comprises determining

whether each metallopeptide induces decreased transmission of the signal.

22. (Original) A method of determining the specific residues binding to a target of interest within a known primary sequence parent polypeptide that binds to the target of interest, comprising the steps of:

(a) making a series of peptides, wherein each peptide in the series includes the known primary sequence of the parent polypeptide with a single substitution, the single substituent consisting of an L- or D-3-mercapto amino acid residue substituted at each position along the primary sequence from the third residue from the N-terminus through the C-terminus residue;

(b) complexing each peptide in the series with a metal ion to form a series of metallopeptides; and,

(c) determining the binding of each metallopeptide of the series of metallopeptides to the target of interest.

23. (Original) The method of claim 22, further comprising the step of selecting the metallopeptide or metallopeptides of the series exhibiting substantially decreased binding to the target of interest.

24. (Original) The method of claim 22, wherein any L- or D-3-mercapto amino acid residue in the series of peptides other than the single substituent L- or D-3-mercapto amino acid residue further comprises a sulfur protecting group, whereby the sulfur therein cannot complex a metal ion.

25. (Original) The method of claim 22, wherein any L- or D-3-mercapto amino acid residue in the series of peptides other than the single substituent L- or D-3-mercapto amino acid residue is substituted with a homolog.

26. (Original) The method of claim 22, wherein for any peptide in the series containing a proline residue as either of the two residues on the immediately adjacent N-terminus side of the

single substituent L- or D-3-mercapto amino acid residue, the proline residue is substituted with a homolog.

27. (Original) The method of claim 22, wherein the L- or D-3-mercapto amino acid is L- or D-cysteine, L- or D-penicillamine, 3-mercapto phenylalanine, or a homolog of any of the foregoing.

28. (Original) The method of claim 22, wherein the metal ion is an ion of V, Mn, Fe, Co, Ni, Cu, Zn, Ga, As, Se, Y, Mo, Tc, Ru, Rh, Re, Pd, Ag, Cd, In, Sn, W, Re, Os, Ir, Pt, Au, Hg, Tl, Pb, Bi, Po, At, Sm, Eu or Gd.

29. (Original) The method of claim 28, wherein the metal ion is an ion of technetium or rhenium.

30. (Original) The method of claim 22, wherein the target of interest is a receptor, antibody, toxin, enzyme, hormone, nucleic acid, intracellular protein domain of biological relevance or extracellular protein domain of biological relevance.

31. (Original) The method of claim 22, wherein determining the binding of each metallopeptide of the series of metallopeptides to the target of interest comprises competing a known binding partner for binding to the target of interest with each metallopeptide.

32. (Original) The method of claim 22, wherein determining the binding of each metallopeptide of the series of metallopeptides to the target of interest comprises a functional assay.

33. (Original) The method of claim 22, wherein the target of interest is a biological receptor capable of transmitting a signal, and wherein determining the binding of each metallopeptide of the series of metallopeptides to the target of interest comprises determining whether each metallopeptide induces decreased transmission of the signal.

34. (Withdrawn) A metallopeptide library for determining the specific residues binding to a target of interest within a known primary sequence parent polypeptide of at least five amino acid residues that binds to the target of interest, comprising:

a series of metellapeptides, wherein each metallopeptide within the series includes the known primary sequence of the parent polypeptide and a single inserted L- or D-3-mercapto amino acid residue, with the single L- or D-3-mercapto amino acid inserted for each peptide at each position along the primary sequence from the position between the second and third residues from the N-terminus through the C-terminus position, and a metal ion complexed to the sequence comprising the single inserted L- or D-3-mercapto amino acid and the two residues on the immediately adjacent N-terminus side of the single inserted L- or D-3-mercapto amino acid residue,

wherein any L- or D-3-mercapto amino acid residue in the series of peptides other than the single inserted L- or D-3-mercapto amino acid residue either further comprises a sulfur protecting group, whereby the sulfur therein cannot complex a metal ion, or a homolog, and further wherein for an metallopeptide in the series containing a proline residue as either of the two residues on the immediately adjacent N-terminus side of the single inserted L- or D-3-mercapto amino acid residue, the proline residue is substituted with a homolog.

35. (Withdrawn) The metallopeptide library of claim 34, wherein the inserted L- or D-3-mercapto amino acid is L- or D-cysteine, L- or D-penicillamine, 3-mercapto phenylalanine, or a homolog of any of the foregoing.

36. (Withdrawn) The metallopeptide library of claim 34, wherein metal ion is an ion of V, Mn, Fe, Co, Ni, Cu, Zn, Ga, As, Se, Y, Mo, Tc, Ru, Rh, Re, Pd, Ag, Cd, In, Sn, W, Re, Os, Ir, Pt, Au, Hg, Tl, Pb, Bi, Po, At, Sm, Eu or Gd.

37. (Withdrawn) The metallopeptide library of claim 36, wherein the metal ion is an ion of technetium or rhenium.

38. (Withdrawn) A metallopeptide library for determining the specific residues binding to a target of interest within a known primary sequence parent polypeptide of at least five amino acid residues that binds to the target of interest, comprising:

a series of metellapeptides, wherein each metallopeptide within the series includes the known primary sequence of the parent polypeptide with a single substitution, the single substituent consisting of an L- or D-3-mercapto amino acid residue substituted at each position along the primary sequence from the third residue from the N-terminus through the C-terminus residue, and a metal ion complexed to the sequence comprising the single substituent L- or D-3-mercapto amino acid and the two residues on the immediately adjacent N-terminus side of the single substituent L- or D-3-mercapto amino acid residue,

wherein any L- or D-3-mercapto amino acid residue in the series of peptides other than the single substituent L- or D-3-mercapto amino acid residue either further comprises a sulfur protecting group, whereby the sulfur therein cannot complex a metal ion, or a homolog, and further wherein for an metallopeptide in the series containing a proline residue as either of the two residues on the immediately adjacent N-terminus side of the single substituent L- or D-3-mercapto amino acid residue, the proline residue is substituted with a homolog.

39. (Withdrawn) The metallopeptide library of claim 38, wherein the substituent L- or D-3-mercapto amino acid is L- or D-cysteine, L- or D-penicillamine, 3-mercapto phenylalanine, or a homolog of any of the foregoing.

40. (Withdrawn) The metallopeptide library of claim 38, wherein metal ion is an ion of V, Mn, Fe, Co, Ni, Cu, Zn, Ga, As, Se, Y, Mo, Tc, Ru, Rh, Re, Pd, Ag, Cd, In, Sn, W, Re, Os, Ir, Pt, Au, Hg, Tl, Pb, Bi, Po, At, Sm, Eu or Gd.

41. (Withdrawn) The metallopeptide library of claim 40, wherein the metal ion is an ion of technetium or rhenium.

RESPONSE

Restriction. The Office Action dated May 2, 2006 asserts the existence of four inventions:

I. Claims 1-9 (in part), and 10-21, drawn to a method for determining the specific residues binding to a target of interest within a known primary sequence parent polypeptide consisting of n residues that binds to the target of interest by insertion of a Z residue.

II. Claims 1-9 (in part) and 22-33, drawn to a method for determining the specific residues binding to a target of interest within a known primary sequence parent polypeptide consisting of n residues that binds to the target of interest by substitution of one the n residues.

III. Claims 34-37, drawn to a metallopeptide library for determining the specific residues binding to a target of interest within a known primary sequence parent polypeptide of at least 5 residues that binds to the target of interest by insertion of a L- or D-3-mercapto amino acid residue.

IV. Claims 38-41, drawn to a metallopeptide library for determining the specific residues binding to a target of interest within a known primary sequence parent polypeptide of at least 5 residues that binds to the target of interest by substitution of one of the residues with a L- or D-3-mercapto amino acid residue.

Election. In response to the Office Action dated May 2, 2006, the Applicants provisionally elect the claims of Group I (claims 1-9 in part and 10-21).

Traverse. Applicant notes that the inventions of Groups I and II are identically classified in the same classes and subclasses. The sole difference between Groups I and II are whether the "Z" residue (a L- or D-3-mercapto amino acid residue) is inserted in the full length parent polypeptide, or whether it is substituted for a single residue in the full length parent polypeptide. Thus the difference is whether, in the practice of the method, the resulting constructs have a length n + 1 (where n is the number of residues in the parent polypeptide) or a length n. With all due deference, Applicant asserts that as a practical matter it would be impossible to conduct a

search that differentiates on this point. Thus Applicant suggests that Groups I and II would not "require different searches", but that the searches would be identically or substantially identically drawn in each instance. If the Examiner, upon reflection, concurs that as a practical matter it would not be possible to implement a search strategy that would produce different results for a method turning on whether the method employs a series of metallopeptides of n length or n + 1 length, then the proper course of action is to withdrawn the restriction requirement as to Groups I and II.

Applicant does not traverse the restriction requirement as to Groups III and IV.

Species of the Invention. At page 5 of the Office Action, it is asserted that the "application contains claims directed to the following patentably distinct species of the claimed invention: a receptor, antibody…" It is respectfully submitted that this statement is not entirely correct. Claim 1 is directed to "[a] method of determining the specific residues binding to a target of interest within a known parent polypeptide that binds to the target of interest…" Claim 5 provides further limitation as to the "target of interest." However, in each instance the invention of claims 1 and 10 are directed to a "parent polypeptide". Thus the invention differs as to the asserted species only as to the "target", or the classification of the binding partner for the parent polypeptide. It is submitted that it is highly unlikely that an individual search as to the binding partner for the parent polypeptide would be fruitful, given that the invention primarily relates to methods of determining the specific residues within a polypeptide that are responsible for binding to the target, where the target may be as appears in claims 5 and 18 for Group I.

It is suggested that the requirement for election of a single species be withdrawn. However, Applicant provisionally elects the species "receptor."

With respect to the assertion that for Group I claims 5 and 18 are generic, Applicant respectfully asserts that claims 1 and 10 are additionally generic. Claims 1 and 10 generically assert a "target of interest", and claims 5 and 18 are dependent claims providing subcategories of a "target of interest."

It is asserted that as to Group I and the provisional election of the species "receptor", all

claims in Group I are readable thereon.

Claim Amendment. Claim 1 is amended to more clearly state the invention. No new matter is added.

Conclusion. Applicant respectfully request that the restriction requirement be reconsidered and withdrawn as to the restriction between Groups I and II, and that claims 1 - 33 of the Application proceed to an examination upon the merits.

If any issues remain, or if the Examiner believes that prosecution of this application might be expedited by discussion of the issues, the Examiner is cordially invited to telephone the undersigned attorney for Applicant at the telephone number listed below.

Authorization is given to charge payment of any additional fees required, or credit any overpayment, to Deposit Acct. 50-3582.

Respectfully submitted,

Date: May 30, 2006

By: /Stephen A. Slusher/
Stephen A. Slusher, Reg. No. 43,924
Direct line: (609) 495-9197

PALATIN TECHNOLOGIES, INC.
4-C Cedar Brook Drive
Cranbury, New Jersey 08512

Telephone: (609) 495-9197
Facsimile: (609) 495-2202

Customer No. 55506